

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
29 September 2005 (29.09.2005)

PCT

(10) International Publication Number  
**WO 2005/089268 A2**

(51) International Patent Classification: Not classified

92009 (US). **CROOKE, Stanley, T.** [US/US]; 3211 Pi-  
ragua Street, Carlsbad, CA 92009 (US).

(21) International Application Number:

PCT/US2005/008428

(74) Agent: **LEGAARD, Paul, K.**; Cozen O'Connor, 1900  
Market Street, Philadelphia, PA 19103 (US).

(22) International Filing Date: 15 March 2005 (15.03.2005)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

60/553,646	15 March 2004 (15.03.2004)	US
60/567,016	29 April 2004 (29.04.2004)	US
60/609,516	13 September 2004 (13.09.2004)	US

(81) Designated States (*unless otherwise indicated, for every  
kind of national protection available*): AE, AG, AL, AM,  
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,  
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,  
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,  
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,  
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ,  
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,  
ZM, ZW.

(71) Applicant (*for all designated States except US*): **ISIS  
PHARMACEUTICALS, INC.** [US/US]; 2292 Faraday  
Avenue, Carlsbad, CA 92008 (US).

(84) Designated States (*unless otherwise indicated, for every  
kind of regional protection available*): ARIPO (BW, GH,  
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,  
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),  
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,  
FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO,  
SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN,  
GQ, GW, ML, MR, NE, SN, TD, TG).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **MIGAWA, Michael,  
T.** [US/US]; 647 Shenandoah Avenue, San Marcos, CA  
92078 (US). **LIMA, Walter, F.** [US/US]; 2405 Bancroft  
Street, San Diego, CA 92104 (US). **SWAYZE, Eric, E.**  
[US/US]; 7789 Palenque Street, Carlsbad, CA 92009 (US).  
**NICHOLS, Joshua** [US/US]; 6842 Via Verano, Carlsbad,  
CA 92009 (US). **WU, Hongjiang** [US/US]; 7831 Calle  
Pinabete, Carlsbad, CA 92009 (US). **PRAKASH, Thazha,  
P.** [IN/US]; 6928 Pear Tree Drive, Carlsbad, CA 92009  
(US). **WYRZYKIEWICZ, Tadeusz, Krzysztof** [PL/US];  
4525 Cove Drive, #2, Carlsbad, CA 92008 (US). **BHAT,  
Balkrishen** [IN/US]; 911 Rosemary Avenue, Carlsbad, CA

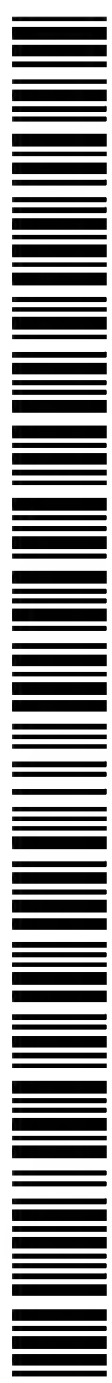
**Published:**

— *without international search report and to be republished  
upon receipt of that report*

*For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.*

(54) Title: COMPOSITIONS AND METHODS FOR OPTIMIZING CLEAVAGE OF RNA BY RNASE H

(57) Abstract: The present invention provides compositions and methods for the optimization of cleavage of RNA species by RNase H. In some embodiments, the invention provides oligonucleotides that possess two or more regions of differing conformation, and at least one transitional nucleobase positioned between the regions that is capable of modulating transfer of the helical conformation characteristic of the region bound to the 3' hydroxy thereof, to the region bound to the 5' hydroxyl thereof.



WO 2005/089268 A2